were observed. After repeated inflations with high pressure the residual area stenosis was reduced only marginally (20 ± 21%; n.s.). Based on IU assessment of the reference area, the balloon size for stent expansion could be increased by at least 0.5 mm diameter in 26% of cases. This lead to an increase of SA_{IU} from 6.30 ± 1.35 mm^2 to 8.40 ± 1.70 mm^2 ($p < 0.001$), and to a reduction of the residual area stenosis to 5 ± 20% ($p < 0.001$). Still, SA_{IU} reached only 77 ± 15% of SA_{BA}. Before IU, only 38% of stents had a residual area stenosis less than 20%; after IU optimization, this fraction of stents was increased to 56%.

After initial high-pressure stent expansion IU revealed a considerable residual stenosis, and in 8% protruding stent struts. The assessment of stents by IU lead to a significant increase of the stent area due to optimized balloon sizes in one fourth of cases. Thus, IU further improved the luminal area gain by stenting even after high pressure deployment.

958-44 Endothelial Hyperplasia and Restenosis Depend on the Technique of Coronary Stent Implantation

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In the animal model of restenosis, the mechanical stretch of artery wall after stent implantation activates smooth muscle cell and endothelial hyperplasia. Therefore the aim of our study was to assess the influence of stent implantation technique on restenosis rate in the population of patients included in BENESTENT I trial.

Methods. 223 patients after primary stent implantation (PS) and 217 after routine coronary angioplasty (PTCA) were included into the study. Quantitative coronary angiogram was performed before and just after the procedure. Additional QCA was taken after 6 month follow-up. From those angiograms reference vessel diameter (Ref1, 2, 3), minimal luminal diameter (MLD1, 2, 3) residual stenosis (ReSt) and luminal diameter stenosis after six months (i.e. restenosis, Rest) were measured. Multivariate regression analysis (MRA) was applied to determine relation of maximal inflation pressure (MaxPress), maximal balloon diameter (Bal) and ratio Bal/Ref1 to late loss of minimal luminal diameter (LL = MLD2–MLD3) and restenosis (Rest).

Results. In both groups of patients significant enlargement of reference diameter was observed after both procedures (Ref1 vs Ref2: $p < 0.001$) and the ratio Ref1/Ref2 correlated well to LL ($r = 0.19$, $p < 0.001$). In PS group, MRA showed that LL was significantly related ($p = 0.0003$, $F = 4.95$, $R = 0.32$) to ReSt (−0.17), Bal/Ref1 (+0.169) and MaxPress (−0.07). Furthermore, the model of Rest ($p = 0.03$, $R = 0.2038$, $F = 3.03$) included: MLD2 (−0.21), Ref1 (+0.114) and MaxPress (−0.09).

Conclusions: To obtain optimal *late result*, high pressure and possibly the smallest balloon diameter giving full stent expansion should be used for coronary stent delivery.

959 Dilated Cardiomyopathy: Molecular Markers and Energetics

Tuesday, March 26, 1996, Noon–2:00 p.m.
Orange County Convention Center, Hall E
Presentation Hour: Noon–1:00 p.m.

959-54 Linkage of Autosomal Dominant Familial Dilated Cardiomyopathy to Chromosome 9

Maja Krajinovic, Bruno Pinamonti, Gianfranco Sinagra, Matteo Vatta, Giovanni Maria Severini, Jelena Milasin, Arturo Falaschi, Fulvio Camerini, Mauro Giacca, Luisa Mestroni, and the Heart Muscle Disease Study Group. *International Centre for Genetic Engineering and Biotechnology, University Hospital, Trieste, Italy*

Idiopathic dilated cardiomyopathy is a heart muscle disease of unknown etiology, characterized by impaired myocardial contractility and ventricular dilatation. Familial transmission is often recognized (FDC), mostly with autosomal dominant inheritance.

In order to understand the molecular genetic basis of the disease, a large six-generation kindred with autosomal dominant FDC was studied for linkage analysis. Eighty family members were investigated and the disease status was established after a clinical follow-up of 3 years. According to strict diagnostic criteria, 13 members were considered to be affected, and 2 of unknown status, while members under the age of 16 were excluded from the linkage study to avoid the low penetrance of this age group. The analysis was then extended to two other informative families with autosomal dominant pattern of transmission and identical clinical features (with 8 affected members, and 1 of unknown status).

A genome wide search was undertaken after a large series of candidate genes were excluded. Co-inheritance of the disease gene was excluded for over 95% of the genome, analyzing 251 polymorphic markers. Linkage was found for chromosome 9q13–q22, with a maximum cumulative two-point lod score of 3.69 (locus d9S153, at $\Theta = 0.08$) and a maximum multipoint lod score of 4.2. There was no evidence of heterogeneity. According to the two-point, multipoint and haplotype analyses, the gene for FDC in these families was placed in the interval between loci D9S153 and D9S152.

A gene for autosomal dominant FDC was localized on the long arm of chromosome 9: several candidate genes for causing dilated cardiomyopathy map in this region.

959-55 A Point Mutation in the 5′ Splice Site of the First Intron of the Dystrophin Gene Responsible for X-Linked Dilated Cardiomyopathy

Jelena Milasin, Francesco Muntoni, Giovanni Maria Severini, Lucia Bartoloni, Matteo Vatta, Maja Krajinovic, Corrado Angelini, Anna Mateddu, Fulvio Camerini, Arturo Falaschi, Luisa Mestroni, Mauro Giacca, and the Heart Muscle Disease Study Group. *International Centre for Genetic Engineering and Biotechnology, University Hospital, Trieste, Italy*

X-linked dilated cardiomyopathy (XLDC) is a familial heart disease presenting in young males as a rapidly progressive congestive heart failure, without clinical signs of skeletal myopathy. This condition has recently been linked to the dystrophin gene in some families, and deletions encompassing the region of the first muscle exon have been detected. In order to identify the defect responsible for this disease at the molecular level, a family with a severe form of XLDC was studied. In the affected members, no deletions of the dystrophin gene were observed. Analysis of the muscle promoter, first exon and intron regions revealed the presence of a single point mutation at the first exon-intron boundary, removing the universally conserved 5′ splice site consensus sequence of the first intron. This mutation introduces a new restriction site for *Mse* I, which cosegregates with the disease in this family. Expression of the major dystrophin mRNA isoforms (from the muscle-, brain- and Purkinje cell-promoters) was completely abolished in the myocardium, while the brain- and Purkinje cell-(but not the muscle-) isoforms were detectable in the skeletal muscle. Immunocytochemical studies with anti-dystrophin antibodies showed that the protein was reduced in quantity but normally distributed in the skeletal muscle, while it was undetectable in the cardiac muscle.

These findings indicate that expression of the muscle dystrophin isoform is critical for myocardial function, and suggest that selective heart involvement in dystrophin-linked dilated cardiomyopathy is related to the absence in the heart of compensatory expression of dystrophin from alternative promoters.

959-56 Angiotensinogen Genotype Is Associated With Myocardial Cell Hypertrophy in Patients With Idiopathic Dilated Cardiomyopathy

Hiroya Sakuramoto, Yoshiyuki Yokota, Motoshi Takeuchi, Hiroya Kawai, Tatsuro Ishida, Tsuyoshi Sakoda, Seinosuke Kawashima, Hozuka Akita, Mitsuhiro Yokoyama. *Kobe University, Kobe, Japan*

Recent in vitro studies demonstrate that angiotensin II causes myocyte hypertrophy and fibroblast proliferation. An angiotensin-converting enzyme (ACE) genotype and angiotensinogen (AGT) genotype have been reported to be associated with heart failure in cardiomyopathy and left ventricular (LV) hypertrophy in hypertension, respectively. However, whether the polymorphisms of these two genes are asscciated with human cardiac histology has not yet been shown. To assess these relations, we studied 44 patients with idiopathic dilated cardiomyopathy (IDC) at the early stage of heart failure. Myocyte transverse diameter (MD) and the extent of fibrosis (%F) were evaluated in endomyocardial biopsy specimens from the interventricular septum of the right ventricle. The polymorphisms of the ACE gene and the AGT gene; M235T and T174M, were determined.

	M174T: TT vs non TT	T235M: TT vs non TT	ACE: II vs ID vs DD
MD (μm)	18 ± 3 vs 23 ± 4§	19 ± 4 vs 20 ± 3	19 ± 3 vs 19 ± 6 vs 19 ± 3
% F (%)	16 ± 2 vs 15 ± 4	15 ± 6 vs 17 ± 6	16 ± 6 vs 17 ± 5 vs 14 ± 7

§$p < 0.001$ vs TT

The T174M variant of the AGTgene ($p < 0.001$) and LV ejectional fraction ($p < 0.05$) were independent predictors of MD by a multiple regression analysis. In conclusion, the T174M variant of AGT gene, but not ACE genotype is associated with myocardial cell hypertrophy in IDC patients.

TUESDAY POSTER